

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
**(PCT Article 36 and Rule 70)**

14.11.2004

Applicant's or agent's file reference 44963/JMD/MR	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA416)
International application No. PCT/GB 03/03575	International filing date (day/month/year) 14.08.2003	Priority date (day/month/year) 14.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K35/23		
Applicant INTERCYTEX LIMITED et al.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the opinion</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>

Date of submission of the demand  14.01.2004	Date of completion of this report  02.11.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Fayos, C  Telephone No. +49 89 2399-2180



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**I. Basis of the report**

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-47                          as originally filed

**Claims, Numbers**

1-44                          as originally filed

**Drawings, Sheets**

1/16-16/16                          as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,        pages:
- the claims,              Nos.:
- the drawings,            sheets:

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5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).  
*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*
6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- the entire international application,
- claims Nos. 1-44 (industrial applicability)  
because:  
 the said international application, or the said claims Nos. 1-44 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):  
**see separate sheet**
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos.
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the Standard.
- the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Yes: Claims	-
	No: Claims	1-44
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-44
Industrial applicability (IA)	Yes: Claims	-
	No: Claims	1-44 see separate sheet

**2. Citations and explanations**

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**see separate sheet**

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**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

- 1- Claims 1-44 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

- 2- Reference is made to the following documents:

- D1: US-A-5 976 524 (HAMMERMAN MARC) 2 November 1999 (1999-11-02) cited in the application
- D2: EP-A-0 853 942 (UNIV WASHINGTON) 22 July 1998 (1998-07-22)
- D3: WO 00 41713 A (ROGERS SHARON A ;UNIV WASHINGTON (US); HAMMERMAN MARC R (US)) 20 July 2000 (2000-07-20)
- D4: ROGERS S A ET AL: 'Transplantation of rat metanephroi into mice.' AMERICAN JOURNAL OF PHYSIOLOGY. REGULATORY, INTEGRATIVE AND COMPARATIVE PHYSIOLOGY. UNITED STATES JUN 2001, vol. 280, no. 6, June 2001 (2001-06), pages R1865-R1869, XP002259735 ISSN: 0363-6119
- D5: HAMMERMAN M R: 'TRANSPLANTATION OF RENAL PRECURSOR CELLS: A NEW THRAPEUTIC APPROACH' PEDIATRIC NEPHROLOGY, SPRINGER VERLAG, BERLIN, DE, vol. 14, no. 6, June 2000 (2000-06), pages 513-517, XP000929752 ISSN: 0931-041X
- D6: ROGERS S A ET AL: 'TRANSPLANTATION OF DEVELOPING METANEPHROI INTO ADULT RATS' KIDNEY INTERNATIONAL, NEW YORK, NY, US, vol. 54, no. 1, July 1998 (1998-07), pages 27-37, XP000929746 ISSN: 0085-2538
- D7: HAMMERMAN M R: 'NEW DEVELOPMENTS IN KIDNEY DEVELOPMENT' NEPHRON, XX, XX, vol. 81, no. 2, 1999, pages 131-135, XP000929750 ISSN: 0028-2766
- D8: ROGERS S A ET AL: 'Transplantation of metanephroi after preservation in vitro.' AMERICAN JOURNAL OF PHYSIOLOGY. REGULATORY, INTEGRATIVE AND

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- COMPARATIVE PHYSIOLOGY. UNITED STATES AUG 2001, vol. 281, no. 2, August 2001 (2001-08), pages R661-R665, XP002259736 ISSN: 0363-6119
- D9: HAMMERMAN M R: 'Growing kidneys.' CURRENT OPINION IN NEPHROLOGY AND HYPERTENSION. ENGLAND JAN 2001, vol. 10, no. 1, January 2001 (2001-01), pages 13-17, XP009020203 ISSN: 1062-4821
- D10: HAMMERMAN MARC R: 'Xenotransplantation of renal primordia.' CURRENT OPINION IN NEPHROLOGY AND HYPERTENSION. ENGLAND JAN 2002, vol. 11, no. 1, January 2002 (2002-01), pages 11-16, XP009020207 ISSN: 1062-4821
- D11: HAMMERMAN MARC R: 'Tissue engineering the kidney.' KIDNEY INTERNATIONAL. UNITED STATES APR 2003, vol. 63, no. 4, April 2003 (2003-04), pages 1195-1204, XP001155987 ISSN: 0085-2538
- D12: HAMMERMAN MARC R: 'Xenotransplantation of developing kidneys.' AMERICAN JOURNAL OF PHYSIOLOGY. RENAL PHYSIOLOGY. UNITED STATES OCT 2002, vol. 283, no. 4, October 2002 (2002-10), pages F601-F606, XP002259738 ISSN: 0363-6127
- D13: HAMMERMAN MARC R: 'Therapeutic promise of embryonic kidney transplantation.' NEPHRON, vol. 93, no. 2, February 2003 (2003-02), pages e58-e62, XP000902020 ISSN: 0028-2766 (ISSN print)
- D14: ROGERS SHARON A ET AL: 'Transplantation of pig metanephroi.' ASAIO JOURNAL (AMERICAN SOCIETY FOR ARTIFICIAL INTERNAL ORGANS: 1992) UNITED STATES 2003 JAN-FEB, vol. 49, no. 1, January 2003 (2003-01), pages 48-52, XP009020205 ISSN: 1058-2916
- D15: LOUGHNA S ET AL: 'A molecular and genetic analysis of renal glomerular capillary development.' ANGIOGENESIS. NETHERLANDS 1997, vol. 1, no. 1, 1997, pages 84-101, XP009020201 ISSN: 0969-6970
- D16: CLARK A T ET AL: 'Molecular regulation of nephron endowment.' THE AMERICAN JOURNAL OF PHYSIOLOGY. UNITED STATES APR 1999, vol. 276, no. 4 Pt 2, April 1999 (1999-04), pages F485-F497, XP002259739 ISSN: 0002-9513

2.1- The relevant passages are those indicated in the search report, unless otherwise specified.

**NOVELTY - Art. 33 (1) and (2) PCT**

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**3- Claims 1-44 lack novelty:**

Note:

The applicant has argued that none of D1-D10 disclose a chimeric kidney located on or near a large blood vessel.

The term "near" is not clear (Art. 6 PCT and PCT guidelines 5.34). The locations of the chimeric kidneys disclosed in D1-D10, are therefore considered to fall within the unclear definition provided in the present claims.

- 3.1- D1: A metanephros from allo- or xenogenic mammalian donor is implanted next to a recipient's omentum or under the renal capsule of the recipient's kidney; method for increasing nephron mass; vascularisation; chimeric kidney that produces urine and develops a ureter.  
D1 is novelty destroying for the subject matter of claims 1-44.
- 3.2- Similarly, D2 (chimeric kidney) is novelty destroying for the subject matter of claims 1-44.
- 3.3- D3: Use of embryonic metanephric tissue to increase functioning renal mass obtained upon transplantation into a recipient; the combination with growth factor is mentioned.  
D3 is novelty destroying for the subject matter of claims 1-44.
- 3.4- D4 relates to the transplantation of rat metanephroi into mice. D4 is novelty destroying for the subject matter of claims 1-7, 10-23, 25-26, 30-38, 40-44.
- 3.5- D5 reviews the use of metanephroi; chimeric kidneys; omentum implantation; vascularisation by arteries originating from the omentum.  
D5 is novelty destroying for the subject matter of claims 1-7, 10-23, 25-26, 30-38, 40-44.
- 3.6- D6 discloses functional chimeric kidneys develop from metanephroi transplanted in adult hosts (subcapsularly in kidneys or into the omentum).  
D6 is novelty destroying for the subject matter of claims 1-7, 10-23, 25-26, 30-38, 40-44.
- 3.7- D7: Transplanted metanephroi become chimeric organs; no use of immunosuppression.

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D7 is novelty destroying for the subject matter of claims 1-7, 10-23, 25-26, 30-38, 40-44.

3.8- D8: implantation of rat metanephroi (E15) into the omentum of nonimmunosuppressed uninephrectomized host rats.

D8 is novelty destroying for the subject matter of claims 1-7, 10-23, 25-26, 30-38, 40-44.

3.9- Similarly, D9 and D10 are both novelty destroying for the subject matter of claims 1-7, 10-23, 25-26, 30-38, 40-44.

**INVENTIVE STEP - Art. 33 (1) and (3) PCT**

4- **No inventive step can be acknowledged for the subject matter of claims 1-44, which is not novel.**

**INDUSTRIAL APPLICABILITY - Art. 33 (1) and (4) PCT**

5- For the assessment of the present claims 1-44 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims.

6- The applicant is reminded that in certain Contracting States the commercial use of embryos (i.e. human embryonic material) is excluded from patentability.